

CLAIMS

sub A3

1. A method for determining whether an individual is likely to have cancer, the method comprising determining a first parameter representing the concentration of TIMP-1 in body fluid samples, and indicating the individual as having a high likelihood of having cancer if the parameter is at or beyond a discriminating value and indicating the individual as unlikely of having cancer if the parameter is not at or beyond the discriminating value.

2. A method according to claim 1, wherein the first parameter is the total concentration of TIMP-1.

3. A method according to claim 1 or 2, wherein the discriminating value is a value which has been determined by measuring said at least one first parameter in both a healthy control population and a population with known cancer, thereby determining the discriminating value which identifies the cancer population with a predetermined specificity or a predetermined sensitivity.

4. A method according to any of the preceding claims, wherein the at least one first parameter determined is the value obtained by combining the concentration of total TIMP-1 with the concentration of free TIMP-1.

5. A method according to claim 4, wherein the combining is performed by logistic regression analysis.

6. A method according to any of the preceding claims, which comprises additionally determining at least one second parameter, the second parameter representing the concentration of an additional marker different from any form of TIMP-1, in a body fluid sample from the individual.

7. A method according to claim 6, wherein the first parameter representing the concentration of TIMP-1 in body fluid samples and the at least one second parameter different from any form of TIMP-1 are combined to result in a combined parameter and indicating the individual as having a high likelihood of having cancer if the combined parameter is at or beyond a discriminating value and indicating the individual as unlikely of having cancer if the combined parameter is not at or beyond the discriminating value.

8. A method according to claim 7, wherein the combining is performed by logistic regression analysis.

5 9. A method according to claim 7 or 8, wherein the discriminating value of the combined parameter is a value which has been determined by determining said combined parameter in both a healthy control population and a population with known cancer, thereby determining the discriminating value which identifies the cancer population with a predetermined specificity or a predetermined sensitivity

10 10. A method according to any of claims 6-9, wherein the at least one second parameter determined is a parameter representing the concentration of a tumour marker.

15 11. A method according to claim 10, wherein the tumour marker is selected from the group consisting of CEA, soluble u-PAR, cathepsin B, HER2-neu, CA15-3 and YKL-40.

12. A method according to claim 11, wherein the at least one second parameter determined is the concentration of CEA.

20 13. A method according to ~~any of the preceding claims~~, wherein the individual is a member of an unselected population.

25 14. A method according to ~~any of the preceding claims~~, wherein the individual is a member of a population already identified as having an increased risk of developing cancer.

30 15. A method for determining whether a patient who has been treated for primary cancer is likely to have metastatic cancer, comprising determining a first parameter representing the concentration of TIMP-1 in body fluid samples, and indicating the individual as having a high likelihood of having metastatic cancer if the parameter is at or beyond a discriminating value and indicating the individual as unlikely of having metastatic cancer if the parameter is not at or beyond the discriminating value.

35 16. A method according to claim 15, wherein the first parameter is the total concentration of TIMP-1.

17. A method according to claim 15 or 16, wherein the discriminating value is a value which has been determined by measuring said at least one first parameter in both a healthy control population and a population with known metastatic cancer, thereby determining the discriminating value which identifies the metastatic cancer population with a predetermined specificity or a predetermined sensitivity.

5
18. A method according to any of claims 15-17, wherein the at least one first parameter determined is the value obtained by combining the concentration of total TIMP-1 with the 10 concentration of free TIMP-1.

19. A method according to claim 18, wherein the combining is performed by logistic regression analysis.

15 20. A method according to any of claims 15-19, which comprises additionally determining at least one second parameter, the second parameter representing the concentration of an additional marker different from any form of TIMP-1, in a body fluid sample from the individual.

20 21. A method according to claim 20, wherein the first parameter representing the concentration of TIMP-1 in body fluid samples and the at least one second parameter different from any form of TIMP-1 are combined to result in a combined parameter and indicating the individual as having a high likelihood of having metastatic cancer if the combined parameter is at or beyond a discriminating value and indicating the individual as 25 unlikely of having metastatic cancer if the combined parameter is not at or beyond the discriminating value.

22. A method according to claim 21, wherein the combining is performed by logistic regression analysis.

30 23. A method according to claim 21 or 22, wherein the discriminating value of the combined parameter is a value which has been determined by determining said combined parameter in both a healthy control population and a population with known metastatic cancer, thereby determining the discriminating value which identifies the metastatic 35 cancer population with a predetermined specificity or a predetermined sensitivity

24. A method according to any of claims 20-23, wherein the at least one second parameter determined is a parameter representing the concentration of a tumour marker.

5 25. A method according to claim 24, wherein the tumour marker is selected from the group consisting of CEA, soluble u-PAR, cathepsin B, HER2-neu, CA15-3 and YKL-40.

10 26. A method according to claim 25, wherein the at least one second parameter determined is the concentration of CEA.

15 27. A method according to any of claims 15-26, wherein the determination is performed at several time points at intervals as part of a monitoring of a cancer patient after the treatment for primary cancer.

25 28. A method according to any of claims 1-14, used for detecting early stage cancer.

30 29. A method according to claim 28, wherein the early stage cancer is selected from the group consisting of colon cancer Dukes' stage A, colon cancer Dukes' stage B, colon cancer Dukes' stage C, rectal cancer Dukes' stage A, rectal cancer Dukes' stage B and rectal cancer Dukes' stage C.

35 30. A method according to any of the preceding claims, wherein the body fluid is selected from the group consisting of blood (serum and plasma), faeces, urine and cerebrospinal fluid.

31. A method according to claim 30, wherein the body fluid is plasma.

32. A method according to claim 30, wherein the body fluid is blood.

33. A method according to claim 30, wherein the body fluid is urine.

34. A method according to any of the preceding claims, wherein the concentration determination is performed by means of an immuno assay or an activity assay.

35. A method according to claim 34, wherein the immuno assay is an ELISA.

M6 36. A method according to claim 34, wherein the activity assay is zymography.

M6 37. A method according to any of the preceding claims, wherein the cancer type is selected from the group consisting of colon cancer, rectal cancer and metastatic breast cancer, lung cancer, prostate cancer, ovarian cancer, cervical cancer, liver cancer and gastric cancer.

WJS

A10

RECEIVED
U.S. PATENT AND TRADEMARK OFFICE